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ATRACTIB: A Phase 2 Trial of First-Line Atezolizumab in Combination with Paclitaxel and Bevacizumab in Metastatic Triple-Negative Breast Cancer

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BACKGROUND

- Based on the results from three phase 3 studies [1-3], taxane-based chemotherapy plus bevacizumab is a widely used regimen as first-line (1L) therapy for metastatic triple-negative breast cancer (mTNBC) in Europe.
- The IMpassion130 and KEYNOTE-355 trials confirmed a substantial benefit from adding an immune checkpoint inhibitor to 1L chemotherapy for mTNBC with programmed death-ligand 1 (PD-L1)–positive tumors [4,5]. However, despite recent advances, many mTNBC patients still have a poor outcome with paucity of alternative treatment options.
- Synergism between antiangiogenic therapy and immunotherapy-based strategies has been shown preclinically and in different tumor types including breast cancer [6-9]. Therefore, this combination should be evaluated in clinical studies in order to improve patient outcomes.
- ATRACTIB evaluates the safety and efficacy of atezolizumab (an anti–PD-L1 antibody) combined with paclitaxel and bevacizumab (a VEGF-targeted drug) as 1L regimen for mTNBC patients irrespective of PD-L1 status.

TRIAL DESIGN

- This is an international, investigator-initiated, open-label, single-arm, phase 2 trial (NCT04408118).
- Patients will be treated with atezolizumab in combination with paclitaxel, and bevacizumab on each 28-day cycle.
- Tumor assessment through computed tomography (CT) scan or magnetic resonance imaging (MRI) will be performed at screening, every 8 weeks during the first 12 months of study drug treatment, and, thereafter, every 12 weeks until progressive disease (PD), withdrawal of consent, start of new anticancer treatment, death, or study termination, whichever occurs first.
- Response will be assessed as best response according to Response Evaluation Criteria in Solid Tumors (RECIST) version (v.)1.1.
- An overview of the study design is shown in Figure 1.

STUDY ENDPOINTS

Primary Endpoint

- To evaluate the efficacy in terms of investigator-assessed progression-free survival (PFS) as per RECIST v.1.1.

Secondary Endpoints

- To assess the efficacy in terms of investigator-assessed objective response rate (ORR), clinical benefit rate (CBR), time to response (TTR), duration of response (DoR), and best percentage of change in target tumor lesions as per RECIST v.1.1; overall survival (OS).
- To evaluate the safety and tolerability of atezolizumab in combination with paclitaxel, and bevacizumab as per National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE) v.5.0.

Exploratory Endpoints

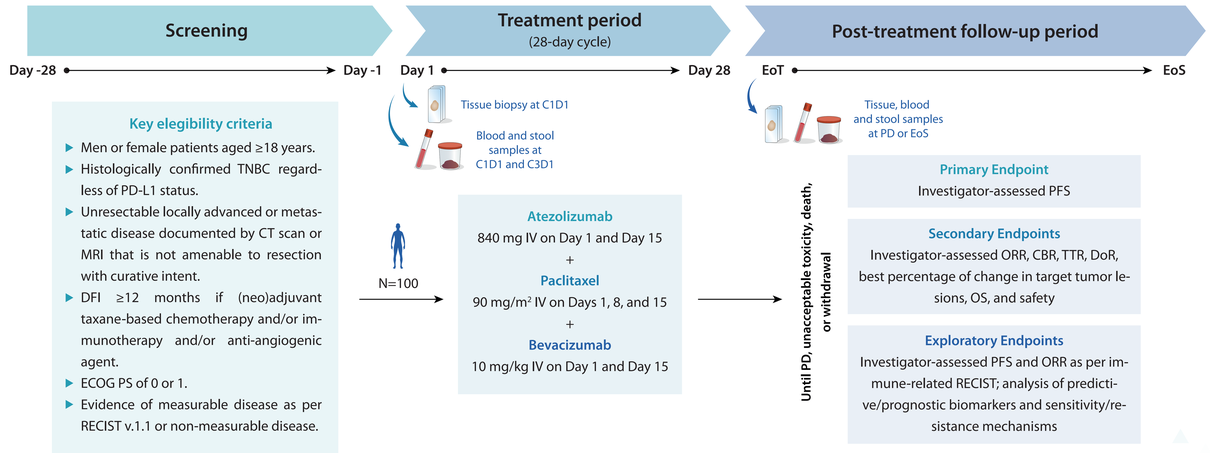
- To assess investigator-assessed PFS and ORR as per immune-related RECIST.
- To investigate predictive and prognostic biomarkers.
- To identify possible mechanisms of sensitivity/resistance to atezolizumab in combination with paclitaxel, and bevacizumab.

STATISTICS

- A sample size of 100 patients is planned.
- The median PFS will be analyzed with exponential maximum likelihood estimation test (Null hypothesis: median PFS ≤7 months; Alternative hypothesis: median PFS ≥9.5 months).
- Based on a 10% dropout rate, a sample size of 100 patients is necessary to attain 80% power at nominal level of one-sided alpha of 0.05.
- An interim analysis for safety and feasibility is planned in the first 20 patients who have completed a 3-month follow-up or have finished the study.

STUDY DESIGN

Figure 1. ATRACTIB Trial Design



Abbreviations: DFI, disease-free interval; ECOG PS, Eastern Cooperative Oncology Group performance status; IV; intravenously; EoT, end of treatment; EoS, end of study.

TRIAL ENROLLMENT

- ATRACTIB was opened to accrual in October 2020.
- It is currently recruiting in 21 institutions across Spain, France, Germany, Italy, and the United Kingdom.

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